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(54) Title: READING OF FLUORESCENT ARRAYS

(57) Abstract: Reading of fluorescent arrays (103) in clinical settings is made possible by a reader (110) constructed to employ dark field illumination of the array, and mapping an image of the array onto a solid state sensor array (146) with image dimensions (D;) of the same order magnitude as the dimensions (D() of the fluorescent array, preferably with reduction of image. High intensity illumination is employed, non uniformities of which being compensated by normalization employing intensity calibration features (164) in the array itself, that are sensed during imaging of the array. Preferably high intensity light emitting diodes (122, 132, 402, 404), such as used in traffic lights, are employed for excitation of the array, preferably the excitation being introduced to the array via a solid internally reflecting homogenizer (130). Intermediate depth of field collection and imaging optics enable substantial collection of light, with NA in the range of 0.30 to 0.60, preferably in the range of 0.4 to 0.55. The resultant relatively large depth of field is in some advantageous cases compensated by absorbing light that tends to travel beyond the spots being imaged and would otherwise create noise fluorescence, the absorption produced e.g., by an opaque metal oxide coating (304) that is interposed between a substrate (302), preferably an ultra-thin substrate, on which the array lies, and the much thicker glass or other rigid support (306). For clinical purposes the arrays comprise fewer than 1000 spots, as is appropriate for protein, one example being an array of fewer than 500 spots. Relatively large spot sizes are employed, i.e. of the order of at least 80 or 100 micron diameter spots or preferably larger, 150 or 300 micron spots. Resolution of such spots to at least 50 pixels on the solid state detector array enables suitable binning and other manipulations leading to highly accurate results. Novel methods of assays and diagnosis such as cancer diagnosis employ the reader in detecting a set of markers related to the disease, for instance ovarian cancer.

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